BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Sylvain V. Costes, Ph.D.	Staff Scientist

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Ecole Nationale Supérieure de Physique de Grenoble	M.S.	1989-1994	Physics & Mathematics
Texas A&M University	M.S.	1993-1994	Nuclear Engineering
University of California, Berkeley Nuclear Engineering Dept	Ph.D.	1996-1999	Nuclear Physics and Radiation Biology (M.H. Barcellos-Hoff, LBNL)
University of California, Berkeley Department of Mathematics	Postdoctoral	1999-2000	Quantitative Radiation Biology (R.K. Sachs)

A. Positions and Honors.

Research Assistant; Nuclear Engineering Dept, Texas A&M Univ., College Station	1993-1994
Research Assistant; Nuclear Engineering Dept, University of Florida, Gainesville	1994-1995
Research Assistant; Nuclear Engineering Dept, Univ. Calif., Berkeley	1996-1999
Postdoctoral Fellow; Dept. of Mathematics, Univ. Calif., Berkeley	1999-2000
Staff Scientist, National Cancer Institute in Frederick, Confocal and Image Analysis Facility	2000-2004
Instructor, Radiation Biophysics at Univ. Calif., Berkeley and NASA summer school	2005-Present
Staff Scientist, Life Sciences Division, Lawrence Berkeley Lab, Univ. Calif., Berkeley	2004-Present

HONORS and PROFESSIONAL SERVICE

1996-1997 **Earl C. Anthony Fellowship and Regents Fellowship**, University of California. 1997-1998 **Outstanding Graduate Student Instructor in Nuclear Physics & Biophysics**, University of California. **Student Travel Award**, Radiation Research Society, 2000. Invited speaker at 35 different scientific meetings, symposiums or seminar. **Outstanding Achievement Award**, Cancer System Biology Division, Lawrence Berkeley Lab, 2008. **Reviewer** for Journal of theoretical Biology, Radiation Research, European Journal of Cell Biology and Cytometry. **Member of** the Radiation Research Society and the American Association for Cancer Research. **Imaging consultant** for Carl Zeiss since July 2006. Member of **Radiation Research Podcast Team** since October 2006.

COMMERCIALIZED ALGORITHM

Automatic co-localization module (3 companies: Improvision (UK), Carl Zeiss (Germany), Bitplane AG (Switzerland)). Costes, S. V. et al. Automatic and quantitative measurement of protein-protein colocalization in live cells. *Biophys J* **86**, 3993-4003 (2004).

B. Selected peer-reviewed publications (16 in chronological order, cited ~500 times).

Costes, S., Streuli, C. H. & Barcellos-Hoff, M. H. Quantitative image analysis of laminin immunoreactivity in skin basement membrane irradiated with 1 GeV/nucleon iron particles. **Radiat Res** 154, 389-97 (2000).

Costes, S. et al. Large-mutation spectra induced at hemizygous loci by low-LET radiation: evidence for intrachromosomal proximity effects. **Radiat Res** 156, 545-57 (2001).

Daelemans, D., Costes, S. V. et al. In vivo HIV-1 Rev multimerization in the nucleolus and cytoplasm by fluorescence resonance energy transfer. **J Biol Chem** (2004).

Costes, S. V. et al. Automatic and quantitative measurement of protein-protein colocalization in live cells. **Biophys J** 86, 3993-4003 (2004).

Daelemans, D., Costes, S. V., Lockett, S. & Pavlakis, G. N. Kinetic and molecular analysis of nuclear export factor CRM1 association with its cargo in vivo. **Mol Cell Biol** 25, 728-39 (2005).

Barcellos-Hoff, M. H. and S. V. Costes "A systems biology approach to multicellular and multi-generational radiation responses." **Mutation Research** 597 (1-2): 32-38 MAY 11 2006

Costes, S. V., A. Boissière, S. Ravani, R. Romano, B. Parvin and M. H. Barcellos-Hoff "Imaging features that discriminate between high and low LET radiation-induced foci in human fibroblasts." **Radiat Res**,165 (5): 505-515 MAY 2006

Fleisch MC, Maxwell CA, Kuper CK, Brown ET, Barcellos-Hoff MH, Costes, S.V."Intensity-based signal separation algorithm for accurate quantification of clustered centrosomes in tissue sections." **Microsc Res Tech** 69 (12): 964-972 DEC 2006

Costes S.V., Ponomarev A., Chen J.L., Nguyen D., Cucinotta F.A., Barcellos-Hoff M.H. "Image-based model reveals dynamic redistribution of DNA damage into nuclear sub-domains", **PLoS Comput Biol.** 2007 Aug 3;3(8):e155- made the cover for the journal for that month

Andarawewa KL, Erickson AC, Chou WS, Costes SV, Gascard P, Mott JD, Bissell MJ, Barcellos-Hoff MH. "Ionizing Radiation Predisposes Nonmalignant Human Mammary Epithelial Cells to Undergo Transforming Growth Factor β Induced Epithelial to Mesenchymal Transition." **Cancer Res.** 2007 Sep 15;67(18):8662-70.

Barkan D, Kleinman H, Simmons JL, Asmussen H, Kamaraju AK, Hoenorhoff MJ, Liu ZY, Costes SV, Cho EH, Lockett S, Khanna C, Chambers AF, Green JE. "Inhibition of metastatic outgrowth from single dormant tumor cells by targeting the cytoskeleton.", **Cancer Res.** 2008 Aug 1;68(15):6241-50.

Maxwell CA, Fleisch MC, Costes SV, Erickson AC, Boissiere A, Gupta R, Ravani SA, Parvin B, Barcellos-Hoff MH: "Targeted and non-targeted effects of ionizing radiation that impact genomic instability" **Cancer Res.** 2008 Oct 15;68(20):8304-11.

Ponomarev AL, Costes SV, Cucinotta FA.: "Stochastic properties of radiation-induced DSB: DSB distributions in large scale chromatin loops, the HPRT gene and within the visible volumes of DNA repair foci", **Int J Radiat Biol.** 2008 Nov;84(11):916-29.

C. M. Ghajar, S. Kachgal, E. Kniazeva, H. Mori, S. V. Costes, S. C. George and A. J. Putnam, Mesenchymal cells stimulate capillary morphogenesis via distinct proteolytic mechanisms. ***Exp Cell Res*** (2010).

S. V. Costes, I. Chiolo, J. M. Pluth, M. H. Barcellos-Hoff and B. Jakob, Spatiotemporal characterization of ionizing radiation induced DNA damage foci and their relation to chromatin organization. ***Mutat Res*** (2010).

R. Mukhopadhya*, S.V. Costes*, A. Bazarov, W.C. Hines, M.H. Barcellos-Hoff, P. Yaswen, Promotion of variant human mammary epithelial cell outgrowth by ionizing radiation: an agent-based model supported by in vitro studies. ***Breast Cancer Research*** (2010)

C. Research Support.

Ongoing

Department of Energy (Costes, Sylvain) 10/01/08-09/30/11

LBNL Low Dose Radiation Program, Project 3: Chromatin Remodeling in Response to Ionizing Radiation

This project examines the effects of ionizing radiation on chromatin composition and organization, and determines the impact of these effects on extracellular signaling-dependent phenotypic transitions in human cells. Dr. Costes group focuses on characterizing by image analysis permanent changes in chromatin organization in primary and immortalized human mammary epithelial cells (HMEC) and fibroblasts at different time points after low and high dose irradiation. This type of studies offers an alternative mechanism for explaining persistent phenotype acquired following exposure to ionizing radiation such as Epithelial-Mesenchymal Transition (EMT) or Genomic Instability (GI).

NASA NSCOR 01/01/09-12/31/14

The contribution of non-targeted effects in HZE cancer risk (Co-PI)

Multi-investigator cross-platform focusing on experimental and modeling studies to define the extent and physiological context in which high LET radiation increases epithelial cancer risk. A large emphasis is made on the non-targeted effect of radiation (intercellular and microenvironment disruption) and how it contributes to cancer. For that effect an agent-based model is developed to encompass genetic modification measured by microarray over large cohort of mice with diverse genotype. Different arrays with time increments covering months following exposure to high and low-LET will be used to predict the response of various organs.

Completed

NNA04CF75I (Barcellos-Hoff, Mary-Helen) 10/01/03-06/30/09

NASA NSCOR *Mechanisms of HZE Damage and Repair in Human Epithelial Cells* (Co-PI)